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(54) **Improved analyzer throughput featuring through-the-tip analysis**

Verbesserung des Analysator-Durchsatzes mittels einer Analyse an der Pipettenspitze

Amelioration de la cadence d'un analyseur en effectuant l'analyse à travers un embout de pipette

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Description

[0001] This invention relates to a method, and a new dispensing station, that allow spectrophotometric analysis to be done on blood samples before they are conventionally tested in a dry or wet assay.

[0002] Spectrophotometric analysis is commonly applied to many liquids to determine the contents. See, for example, US-A-4420254, the disclosure of which forms the basis for the preamble of claims 1 and 11. Such analysis is particularly useful if done with near infrared radiation, due to the latter's ability to discriminate between a target analyte and other substances.

[0003] That such analysis is possible to ascertain hemoglobin, glucose, albumin, lipids, and many other sera components is evident from, for example, Clin. Chem., Volume 38, Pages 1623-1631 (1992).

[0004] Problems have existed, however, in applying such analysis to blood samples to determine the contents or quality of such samples. It has been difficult, for example, to apply it to samples as they are obtained initially, namely in primary patient collection containers. These are usually tubes of varying size that have been centrifuged to separate the liquid serum or plasma from the cellular phases. Such tubes therefore have a) a patient-identification label, b) varying and unpredictable locations of the sera to be analyzed, and c) a large amount (milliliters) of sample required. As to the varying locations, the gel barrier used to separate the liquid phase from the cellular phase, if scanned instead of the liquid phase, no doubt will produce an incorrect evaluation.

[0005] Thus, it has been the practice, when dealing with tubes of liquid of unpredictable height, to aliquot into a secondary tube, with added exposure and time, or ascertain where the liquid phase is, such as by LED scanning of the tube contents, as shown, for example, in Fig. 3 of EPA 185,330. Such requirements introduce additional equipment expenses and process delays. This, coupled with the difficulties of spectrophotometrically scanning through the patient label, has rendered such scanning of primary collection containers problematic and expensive.

[0006] On the other hand, conventional clinical analyzers using dried slide test elements to test for target substances, require usually at least five minutes to conduct an assay of the target substance, given the need for incubation. With these incubator times, it becomes difficult to obtain throughputs much greater than 1000 tests per hour. A technique that would allow for much higher throughput in such analyzers is sorely needed.

[0007] Thus, there has been a problem prior to this invention, of providing an inexpensive and simple method of spectrophotometric scanning of biological liquids such as blood sera or plasma separated from whole blood, that is, one which eliminates the need to locate the liquid's position in whatever container is used, and the need to scan through an identification label. There is further a need to enhance the throughput of tests in an analyzer that assay target substances.

[0008] The above-noted problem is solved by this invention in part by a method for improving throughput in a clinical analyzer as defined in claim 1, the analyzer comprising a dispensing station and at least one test station for detecting a target substance in a patient sample, the dispensing station comprising: an aspirator probe; a tip mounted on the probe, for collecting a biological liquid from a primary collection container and for dispensing at least a portion of the collected liquid onto or into a test element; and means for creating a partial pressure or partial vacuum within the probe and the tip.

[0009] Still another aspect of the solution of the problem features a dispensing station for use in a clinical analyzer as defined in claim 11. Accordingly, it is an advantageous feature of the invention that throughput of assays of target substances in an analyzer is increased.

[0010] Yet another advantageous feature is that results are achieved in less time since no incubation time is required for the spectrophotometric analysis.

[0011] Other advantageous features will become apparent upon reference to the following description, when read in light of the attached drawings.

Fig. 1 is a fragmentary isometric view of an analyzer aspirator probe, illustrating the location of the scanning block of Figs. 2A and 2B in the rest of a conventional analyzer;

Figs. 2A and 2B are alternative fragmentary elevational views in mid-section of the apparatus providing two alternative embodiments of the invention;

Fig. 3 is an isometric view, partially broken away at its mid-section, of the station 82 of Fig. 2A, showing the air vent that prevents both a pulse of upward pressure from occurring when the tip is inserted, and suction on the end of the tip when the tip is removed;

Fig. 4 is a fragmentary isometric view of light-tight enclosures which can be used in the method of the present invention.

Fig. 5 is a plan view in section of a portion of the structure of Fig. 4, illustrating a mechanism for locating tip 48A;

Figs. 6 through 11 are regression plots of test samples scanned and analyzed spectrophotometrically in accordance with the invention, for levels of hemoglobin, lipemia, or icteric nature of the sample;

Fig. 12 is a plot of spectral transmissions detected by the invention, showing a sample of each of icterus, hemoglobin

and lipids;

Figs. 13 and 14 are fragmentary elevational views similar to that of Fig. 2A, Fig. 13 illustrating how to transmit light through the tip in more than one pass, and Fig 14 illustrating how light can be transmitted through the narrower neck portion of the tip; and

Figs. 15 and 16 are regression plots of test samples scanned and analyzed spectrophotometrically in accordance with the invention, for levels of bilirubin.

[0012] The invention is hereinafter described in connection with preferred embodiments, in which a preferred (and conventional) translucent disposable tip is used on a preferred (and conventional) analyzer aspirator, and a preferred light-tight enclosure connected to the spectrophotometer by passageways using fiber optics, to analyze for targets representing patient sample quality in blood serum or plasma. Additionally, however, the invention can be used regardless of the type of translucent or transparent tip, aspirator, liquid, or light-tight enclosure that is used, regardless of the optical system providing passageway of the light to and from the spectrophotometer, and regardless of the target substance being detected, so long as the target has sufficient NIR and adjacent visible radiation absorption. That is, the target substance can be a traditional substance tested for concentration in an analyzer heretofore on a slide test element, for example, albumin or glucose. The liquid can be whole blood, urine or cerebral spinal fluid as well. Also, the tip can be permanent rather than disposable, and an open lens system could be used in place of fiber optics, to focus the light to the light-tight enclosure and then to the detecting station.

[0013] Not shown herein nor described in any detail is the spectrophotometer used with the invention. The reason is that any spectrophotometer is useful, provided it generates and detects via transmission, radiation emitted in the near infrared and adjacent visible light regions with sufficient spectra precision. As used herein, "near infrared and adjacent visible" means, radiation between 400 and 2500 nm, and most preferably, between 475 and 1075 nm. These wavelengths are advantageous as they provide sufficient spectral penetration of the disposable tip as well as sufficient spectral absorption from target analytes. 475 nm is considered to be particularly useful for bilirubin detection by this invention. Useful materials for the tips that allow desired spectral penetration are those commonly used to manufacture disposable tips (polypropylene or polyethylene).

[0014] Also as used herein, "spectrophotometric" means a technique that captures the spectral response over a range of wavelengths and correlates a response for each wavelength in the range. In contradistinction, "photometric" means an analysis of light radiation to correlate a response to only a particular wavelength. A "spectrophotometer" then is the apparatus that does this spectrophotometric analysis.

[0015] Also, as used herein, "primary patient collection container" means, a container in which patient biological liquid, usually blood, is placed initially, with a label, and processed to prepare the desired sample liquid for testing. In the case of whole blood, such processing includes phase separation in which liquid serum or plasma is separated from the cellular phase comprising the blood cells, usually with a gel separation barrier.

[0016] Further, as used herein, a "test element" means any reaction vessel in which at least one reagent has been pre-supplied, for example so-called dried slide test elements such as are described in, for example, US-A-3,992,158; or a cup or well having a cavity pre-coated with one or more antibodies, such as is described in US-A-5,441,895, or an uncoated cavity to which reagent is added.

[0017] Further as used herein, "light tight" means, effective to exclude ambient light by an amount such that no more than 10 percent of the detected light is due to the exterior ambient light.

[0018] Still further as used herein, "icteric" means the condition wherein high levels of bilirubin and/or biliverdin are present in the sample.

[0019] No details are provided as to the mathematical analysis involved in correlating the amount of transmission of the near infrared and adjacent visible radiation through the biological liquid, with the concentration of the target substance. The reason is that such is well-known, as is evident from Canadian Patent No. 2,019,511; the article in Clin. Chem., Volume 38, Pages 1623-1631 (1992); and the tutorial articles in Anal. Chem., Volume 59, Number 17, Pages 1007A-1017A (9/1987) and Anal. Chem., Volume 66, Number 15, Pages 795A-804A (8/1994).

[0020] Fig. 1 illustrates a conventional analyzer 12 utilizing the current invention. It is conventional to utilize a dispensing station 18 to collect by aspiration, a sample of biological liquid, for example, serum or plasma, from a supply comprising primary collection containers 19 in tray 20, into a disposable tip 48 mounted on aspirator probe 46. The sample liquid is subsequently dispensed onto a slide test element E held at a slide distributor 30 and obtained from a source of test elements, not shown. Control of the dispenser 40 providing probe 46 is via the mechanisms such as vertical drive 44 and carriage 42 mounted on support rods 70, all as described in, for example, US-A-4,340,390. A conventional pump 71 of any kind is used as the means for creating a partial vacuum or partial pressure within tip 48.

[0021] A new use is made of tips 48 besides simply, the collection by aspiration, of liquid from containers 19, and then subsequent dispensing onto slide test elements E. Tip 48 carrying the sample liquid aspirated into it, is moved, arrow 80, Fig. 1, to a test station 82 prior to placing it in holder 117 for dispensing. Station 82 comprises, as is more clearly shown in Figs. 2A, 2B, and 3, a scanning block that is an effective light-tight enclosure having a cavity 84 sized

to receive a tip 48. Preferably, cavity 84 comprises an upper portion 86, Fig. 3, a lower portion 88 of smaller inside diameter than portion 86, a ledge 90 of demarcation between the upper and lower portions, an air vent 92 in ledge 90, a conical exit port 94 extending from the lower portion away from the upper portion, and two passageways 96 adapted to receive fiber optics 98,98' to and from portions of a spectrophotometer. Exit port 94 is shaped generally with the shape of the exit orifice portion of tip 48, hence its conical shape for this preferred tip 48. An optional air tube 100 is connected to exit port 94 to reduce the potential of pumping fluid out of the tip. If the tube is also opaque, an option, then it also helps to eliminate light leakage up into the tip.

[0022] Fiber optics 98,98' are connected to a spectrophotometer, Fig. 1, comprising a light source 110 and a detector combined into a single unit 110, which is conventional.

[0023] For maximum efficiency, station 82 is effectively light-tight as defined herein so that the light passing to the detector is at least 90% of that transmitted through tip 48 from fiber optic 98. There are several ways in which this can be achieved.

[0024] First, for a station 82 as shown in Fig. 2A, comprising block 83 having an upper surface 90 that acts as the support shoulder for the enlarged upper portion 111, and hence goes no higher than that, and a side clearance of 0.5 mm between tip 48 and block 83, the light leakage that occurs is corrected for by taking a blank reading (with the fiber 98 delivering no light) at the same ambient light conditions as is used when NIR and adjacent visible radiation is delivered by fiber optic 98. The blank reading is then subtracted from the sample reading and reference reading.

[0025] Alternatively, if a subtracted blank reading is not to be used, and the side clearance is still the same as noted above, the same light tightness can be achieved by extending the height of block 83 up to at least the height of the top surface 113 of upper portion 111 of tip 48, Fig. 2B.

[0026] Because the seating of tip 48 on shoulder surface 90 is an effective seal, some air release is provided between upper and lower portions 86 and 88 as tip 48 is inserted and withdrawn. That is the function of vent 92, Fig. 3. This vent allows the release of the increase in pressure created when a tip is inserted into station 82, so that a bubble of air is not forced into the liquid of the tip to possibly interfere with the light-scanning of the liquid. Likewise, when tip 48 is withdrawn after having been light-scanned, vent 92 prevents a vacuum being created such as could draw out of tip 48, a portion of the sample liquid which then contaminates the station 82 for subsequent tips and samples.

[0027] To further assist in centering tip 48 within cavity portion 88 between fiber optics 98 and 98', locator bumps 140 can be disposed, Fig. 3, near the bottom of portion 88 above passageways 96.

[0028] In use, tip 48 is inserted into station 82 before insertion into holder 116. While at station 82, a beam of NIR and adjacent visible wavelengths as defined above, is passed through the tip and its liquid so that transmitted radiation is spectrophotometrically analyzed at spectrophotometer 110. The signal produced by the detector is then correlated with the concentration of target substances. A preferred set of target substances is those that measure sample quality, specifically those selected from the group consisting of hemoglobin, lipids, bilirubin (BR), and biliverdin (BV), as shown in the examples below. However, any target substances capable of spectrophotometric detection by its absorption spectra, can be correlated and detected by this invention. More specifically, certain assays that heretofore have been conducted in slide test element E, can be conducted spectrophotometrically through the tip, as described hereinafter.

[0029] Thereafter, the tip is withdrawn and inserted into holder 116 at which point the sample liquid is dispensed onto slide test element E conventionally containing one or more reagents to ascertain the concentration of an analyte in the sample liquid, as is well-known.

[0030] As will be readily evident, the tips 48 used herein allow transmission of NIR and adjacent visible radiation, and most preferably 475 to 1200 nm, and preferably are free of labels, since any labeling is done exclusively on primary containers 19. Materials useful for this purpose include polypropylene and polyethylene.

[0031] It is not necessary that test station 82 used in the method of the present invention be constructed as a solid block with only a cavity for the disposable tip and apertures for the fiber optics, or that the tip be lowered into the same. Instead, side walls of station 82 can be opened and closed, to provide a slot that allows pass-through of the tip, as shown in Figs. 4A and 5. Parts similar to those previously described bear the same reference numeral, to which the distinguishing suffix "A" has been appended.

[0032] Thus, station 82A comprises two fixed, opposed segments 109,112 spaced a distance apart. Each segment has an opposing face, 116,116' that defines a slot 115 between them. Top surface 117 of faces 116,116' provide a guide rail and seat for upper portion 111A of tip 48A. Segment 109 has a fiber optic 98A penetrating it from a light source, not shown, whereas segment 112 has a sensor 114 in face 116 that is connected to a spectrophotometer built into or connected with segment 112.

[0033] The opposing faces of segments 109 and 112 define slit 115 with a spacing distance that allows a disposable tip 48A to slide through, arrow 120. Those opposing faces can be spaced apart a fixed distance for the sliding of tip 48A.

[0034] Because segments 109 and 112 create slot 115 for the through-passage, arrow 120, of tip 48A, with an aspect ratio much smaller than that described above for the vertical aperture 84, it is preferred to close slot 115 for the spectrophotometric measurement. To that end, pivoting doors 130,132 are hingedly attached at 134 to opposite edges of segment 109, of sufficient width to close off slot 115 when they are pivoted, arrows 136,138 to their closed positions

(not shown). (Door 132 is shown in phantom for clarity only.) To pivot the doors, preferably the pintle of hinges 134 is attached or affixed to a rotating drive shaft (not shown), of conventional motors 136.

[0035] Alternatively, doors 130 and 132 can be omitted by lengthening slot 115 so that it has an aspect ratio in the horizontal direction that is comparable to the vertical aspect ratio stated for cavity 84 above.

[0036] To assist in stopping the lateral movement, arrow 120, of tip 48A just precisely at fiber optic 98A and detector 114, Fig. 5, a spring-biased detent 210 is preferably located in face 116, cooperating with a fixed projection 212 on opposite face 116'. Detent 210 is pushed by the tip into face 116 when it is time, after the reading, to move tip 48A out of slot 115 in the direction of arrow 120. As noted in the previous embodiment, tip 48A allows transmission of the NIR and adjacent visible wavelengths used.

[0037] Alternatively, Fig. 4B, segment 112B can be movably mounted on plate 122B to close off light leakage. Parts similar to those previously described bear the same reference numeral, to which the distinguishing suffix "B" is appended. Thus, station 82B comprises plate 122B forming with faces 116B and 116'B a U-shaped slot that allows a tip 48B to slide through, arrow 120B, while supported on top surfaces 117B. Fiber optic 98B delivers light through stationary segment 130B, and sensor 114B in stationary face 116B delivers light to a spectrophotometer, not shown.

[0038] To close the light leakage that can occur through the U-shaped slot of plate 122B and faces 116B and 116'B, segment 112B is mounted to slide on plate 122B as driven by a rack 162 and a drive pinion 164, arrow 168, thus opening or closing off the slot. When closed, face 116B and tip 48B occupy the space 172 within segment 112B, and wall portion 169 closes off slot 115B.

[0039] In addition to testing for patient sample quality, any target substance that is analyzable spectrophotometrically using NIR and adjacent visible wavelengths, can be analyzed by spectrophotometer 110 while the patient sample is in tip 48A. These include hemoglobin, albumin, and glucose, among others. By testing these target substances in,the tip, it is not necessary, and indeed the analyzer preferably skips, further assays for them when the sample is deposited onto slide test element E. This enhances greatly the total throughput of the analyzer, inasmuch as the spectrophotometric detection through the tip requires only 4 seconds for all the target substances so analyzed, compared to 4 seconds for each separate assay done on a slide test element E. "Time to result" is also drastically improved by the spectrophotometric analysis through the tip - 4 seconds for through-the-tip, compared to 5 minutes on a slide test element.

[0040] As an example of the enhanced throughput, the following is a calculation of the advantages that can be achieved on an analyzer such as is available from Johnson & Johnson Clinical Diagnostics under the trademark "VITROS 950" analyzer. This assumes 1) that dispensing of sample liquid onto a slide test element is the limiting step in the analysis, and that this involves 8 seconds to aspirate, 4 seconds to dispense onto a test element and load the element into the distributor of the VITROS 950 analyzer, and that all, and only, colorimetric analysis is done in the tip by this invention.

[0041] If the mix of chemistries to be run is zero potentiometric, 7 colorimetric and zero rates, then without the invention the throughput is 300 test elements per hour. With the invention, it can be shown to be 2100 per hour, which is a 7-fold increase. If on the other hand there are only 5 colorimetric tests, and either 2 rate or 2 potentiometric tests to be conducted, then the throughput without the invention should be 420 per hour, and 1050 per hour with the invention, for a 2.5-fold increase. Still further, if the mix of seven chemistries is such that there are only 3 colorimetric and 4 potentiometric tests to run, there is no increase in throughput obtained by doing this invention (525 tests per hour in both cases.)

[0042] Testing of such analytes in this manner while in the tip is preferably done with some kind of temperature control of the sample liquid. This need not be done only by controlling the temperature at test station 82, but can also be done by heating or cooling the sample liquid in containers 19, Fig. 1, or while the liquid is in the tips 48, and so forth, but not at station 82.

[0043] Nevertheless, there will still be some assays that require the use of slide test element E. The process is schematically illustrated in Fig. 1. Tip 48 is inserted into holder 117 and a portion of the patient sample is dispensed onto slide test element E. Thereafter, distributor 30 is rotated, arrow 140, to a position in which test element E is linearly transferred, arrow 142, to an incubator (not shown) within which it rotates, arrow 144, until it is read or detected at a test station 146, all as is well-known and conventional. Test station 146 conventionally comprises a colorimetric or potentiometric detector, in contrast to the spectrophotometer 110 used with tips 48,48A.

[0044] Although as noted above, tests conducted at station 146 preferably skip those done through the tip, it is also possible to repeat at station 146 such spectrophotometric assays, to obtain a "check" on the accuracy of the latter.

[0045] It is also contemplated that the order of testing can be reversed - that is, a portion of the sample liquid can be deposited on a test slide as described above, before doing the measurements through-the-tip at the NIR and adjacent visible wavelengths.

Examples

[0046] The following non-exhaustive tests were run to demonstrate the invention:

[0047] The apparatus of Fig. 2 was used, in which a disposable tip available from Johnson & Johnson Clinical Diagnostics, Inc., under the trademark "Vitros", heretofore known as the "Ektachem" disposable tip, was used. The optical fibers were 0.2 mm single fibers, connecting station 82 via the fibers 98 and 98', to a "TC 2000" dual beam, in-time spectrophotometer that uses a linear diode array detector, available from CME Telemetrix, using a tungsten-halogen light bulb light source 110 as detector 112. Diffraction gratings were used at detector 112 to allow only radiation of 580 to 1100 nm to be detected. (The reference beam portion of the spectrophotometer has been omitted for clarity.) The amount of liquid aspirated into tip 48 was 50 μL, so that the liquid level was well above the pass-through arrow 200, Fig. 2. Testing has demonstrated that only 30 μL is needed.

[0048] The liquids tested were, first as calibrators, a randomized set of liquids comprising known amounts of hemoglobin, Intralipid™ (a fat emulsion which mimics naturally occurring chylomicrons) available from Pharmacia, Inc., and biliverdin all spiked onto a human serum matrix.

[0049] The following Table 1 sets forth the levels of Hb, IL, and BV in serum after spiking. "Hb" means hemoglobin, "IL" means Intralipid, "BV" means biliverdin dihydrochloride, and "BR" means bilirubin.

TABLE 1

Sample Number	g/L Hb	g/L IL	mg/dL BV
1	0.56	0.00	0.00
2	0.83	0.00	0.00
3	1.11	0.00	0.00
4	1.38	0.00	0.00
5	1.65	0.00	0.00
6	1.91	0.00	0.00
7	2.17	0.00	0.00
8	2.43	0.00	0.00
9	2.69	0.00	0.00
10	2.95	0.00	0.00
11	1.19	0.00	0.00
12	1.77	0.00	0.00
13	2.35	0.00	0.00
14	2.93	0.00	0.00
15	3.50	0.00	0.00
16	4.06	0.00	0.00
17	4.62	0.00	0.00
18	5.17	0.00	0.00
19	5.71	0.00	0.00
20	6.26	0.00	0.00
21	0.54	1.00	0.83
22	0.79	1.97	0.41
23	1.01	2.83	1.17
24	1.22	1.14	3.77
25	1.50	1.63	2.32
26	1.73	2.30	1.91

TABLE 1 (continued)

Sample Number	g/L Hb	g/L IL	mg/dL BV
27	2.03	1.42	1.57
28	2.25	0.47	2.70
29	2.46	0.68	3.03
30	2.54	3.00	3.21
31	1.14	2.00	1.66
32	1.69	3.94	0.82
33	2.13	5.61	3.10
34	2.59	2.27	7.55
35	3.19	3.26	4.63
36	3.68	4.61	3.82
37	4.36	2.86	2.37
38	4.78	0.93	5.40
39	5.22	1.37	6.06
40	5.40	6.01	6.41

[0050] A second set of 21 liquids similarly prepared, were prepared to have the components of Table 2, and treated as unknowns.

TABLE 2

Sample Number	g/L Hb	g/L IL	mg/dL BV
1	0.34	2.05	3.40
2	0.50	2.44	4.06
3	0.66	2.83	4.69
4	0.80	3.19	5.30
5	3.77	3.27	5.43
6	1.08	3.88	6.44
7	1.35	1.56	3.33
8	1.56	1.15	1.15
9	5.73	3.04	2.21
10	1.80	3.04	1.80
11	4.75	3.54	1.31
12	2.12	2.60	2.16
13	2.18	4.13	2.74
14	2.58	0.46	0.76
15	5.26	1.55	4.50
16	2.68	1.26	5.56
17	2.83	0.83	6.23
18	0.00	2.38	0.00
19	1.79	0.00	0.00

TABLE 2 (continued)

Sample Number	g/L Hb	g/L IL	mg/dL BV
20	0.00	0.00	3.95
21	0	0	0

[0051] The first set of liquids was irradiated as described above to create a calibration algorithm using conventional spectrophotometric practice, and the values of Hb detected in this measurement were plotted against the actual values, Fig. 6, to obtain a regression plot. A variety of calibration algorithms is useful. The following equations are exemplary only:

1)

$$Hb(g/l)\ C_1(dA_{600}/d\lambda_{600}) - C_2(dA_{663}/d\lambda_{663}) - C_3$$

2)

$$IL(g/l) = C_4(dA_{874}/d\lambda_{874}) + C_5$$

3)

$$BV(mg/dL) = C_6(dA_{724}/d\lambda_{724}) - C_7(dA_{803}/d\lambda_{803}) + C_8$$

where A_{600} is the absorbence at 600 nm, λ_{600} is the 600 nm wavelength, and so forth for the other A + λ values, ($dA_i/d\lambda_i$) is the first derivative of absorbence versus wavelength and C_1, ... C_9 are constants preferably having the following values:

$C_1 = 15.892$	$C_5 = 0.244$
$C_2 = 15.882$	$C_6 = 98.068$
$C_3 = 0.21$	$C_7 = 122.732$
$C_4 = 252.155$	$C_8 = 0.0685$

[0052] The regression correlation coefficient R^2 in the case of Fig. 6 was 0.991.

[0053] The second set of liquids was then irradiated as described above and the predicted values plotted against their known results, Fig. 7, using the calibration algorithm derived from the first set of liquids, Fig. 6. The R^2 value of 0.982 was excellent. This accuracy is adequate to allow the results to be relied upon for clinical assay of Hb in unknown samples, in place of testing on a slide test element.

[0054] In a like manner, the spectra detected as noted above was evaluated for IL. The calibration results appear in Fig. 8, and the prediction results in Fig. 9. R^2 in this case was, respectively, 0.9941 and 0.9878.

[0055] Again, the spectra noted was evaluated, but this time the analysis was for BV. Fig. 10 shows the calibration results, and Fig. 11 the prediction results with R^2 being as indicated.

[0056] A new, third set of liquids was prepared to illustrate the invention in the detection of bilirubin, and the calibrator version of that set was composed as follows:

Sample Number	BR mg/dL	Hb g/L	IL gL	BV mg/dL
1	8.33	0.65	0.00	0.00
2	8.33	0.65	0.00	0.00
3	0.00	1.92	0.00	0.00
4	0.00	1.92	0.00	0.00
5	34.79	0.91	0.00	0.00

(continued)

Sample Number	BR mg/dL	Hb g/L	IL gL	BV mg/dL
6	34.79	0.91	0.00	0.00
7	23.41	1.53	0.00	0.00
8	23.41	1.53	0.00	0.00
9	31.49	0.31	0.00	0.90
10	31.49	0.31	0.00	0.90
11	37.33	1.17	0.00	1.72
12	37.33	1.17	0.00	1.72
13	22.15	0.00	0.93	0.00
14	22.15	0.00	0.93	0.00
15	0.00	0.00	2.15	0.00
16	0.00	0.00	2.15	0.00
18	17.02	0.00	0.00	8.74
19	17.02	0.00	0.00	8.74
20	33.31	0.00	0.00	1.80
21	33.31	0.00	0.00	1.80
22	25.02	0.00	0.00	5.34
23	25.02	0.00	0.00	5.34
24	29.13	0.00	0.00	3.58
25	29.13	0.00	0.00	3.58
26	13.59	0.00	0.00	7.18

[0057] The calibration algorithm used for this test was as follows:

4)

$$BR(mg/dL) = C_9(dA_{495}/d\lambda_{495}) + C_{10}(dA_{512}/d\lambda_{512}) + C_{11}(dA_{578}/d\lambda_{578}) - C_{12}$$

wherein the constants were as follows:

$C_9 = -24.878$
$C_{10} = 201.61$
$C_{11} = 44.98$
$C_{12} = 6.475$

[0058] A fourth set of liquids was similarly prepared to check for prediction of the bilirubin values, and that set was comprised as follows:

Sample Number	BR mg/dL	HB	IL	BV mg/dL
1	19.86	1.25	0.00	0.00
2	19.86	1.25	0.00	0.00
3	26.59	0.60	0.00	4.38

(continued)

Sample Number	BR mg/dL	HB	IL	BV mg/dL
4	26.59	0.60	0.00	4.38
5	6.10	0.00	2.35	0.00
6	6.10	0.00	2.35	0.06
7	10.31	0.00	1.19	0.00
8	10.31	0.00	1.19	0.00
9	15.53	1.07	0.00	3.58
10	15.53	1.07	0.60	3.58

[0059] The spectra was evaluated as in the previous examples. Fig. 15 shows the calibration results, and Fig. 16 the prediction results with R^2 being as indicated.

[0060] For all four experiments (Hb, IL, BV and BR) the results showed excellent correlation such that the results are sufficient to use in place of testing on a slide test element, should any of these be considered a desired assay. In any event, the results clearly allow the biological liquid's sample quality to be ascertained so that the sample can be rejected if determined to be outside the scope of acceptable quality.

[0061] As an example of other calibration algorithms that can be used, the following is an alternative to equation #2 above, for IL:

2')

$$IL(g/l) = C_{13}(dA_{999}/d\lambda_{999}) + C_{14}(dA_{1051}/d\lambda_{1051}) - C_{15},$$

where C_{13} = 166.068, C_{14} = 92.352, and C_{15} = 0.693. When this is used on the first and second set of liquids noted above, R^2 becomes 0.988 for the calibration and 0.984 for the prediction. (The actual plots are not shown.)

[0062] Fig. 12 is a plot demonstrating that, in fact, the first derivative of absorbence values in the NIR and adjacent visible spectra does produce sufficient separation, at useful wavelengths, of a sample having either IL, BV, or Hb components present, to allow for independent detection. That is, curve 200 is a sample having none of those components, curve 202 is a sample having only 1.79 g/l of Hb, curve 204 of a sample having only 2.38 g/l of IL, and curve 206 of a sample having only 3.95 mg/dL of BV. Thus, the Hb contributes primarily to the 580-605 nm region of the NIR, IL to the 896-1051 nm region and preferably 896-939 nm, and BV to the 680-750 nm region.

[0063] In an example useful for understanding claims 4 and 14 of the present invention, the tip is unchanged from conventional tips, but more than a single pass of the NIR and adjacent visible radiation is achieved through the tip before the absorption spectra is received by the spectrophotometer, Fig. 13. Parts previously described are referred to by the same reference numeral, to which the distinguishing suffix "D" is appended.

[0064] Thus, tip 48D is mounted in cavity 84D as before, for irradiation by NIR and adjacent visible radiation emanating from fiber optic 98D, to be received by fiber optic 98'D for processing. However, unlike previous embodiments, receiving optic 98'D is not directly opposite transmitting optic 98D, nor in position to receive the "first pass" radiation. Instead at least one, and preferably three pair(s) of mirrors (230,232; 240,242; and 250,252) are disposed to re-pass the radiation back through tip 48D as many times as there are mirrors. (Six mirrors of the three pairs retransmits the radiation through the tip six times.)

[0065] It is not necessary that optics 98,98' (or other versions thereof disclosed above) pass NIR and adjacent visible light through only the thickest part of the tip. Instead, in accordance with the method of the present invention, the light is transmitted through the narrower neck portion. (Parts similar to those previously described bear the same reference numeral, to which the distinguishing suffix "E" is appended.)

[0066] Thus, Fig. 14, illuminating fiber optic 98E is positioned in the block of station 82E so as to illuminate conical neck portion 300 of tip 48E, that has a decreasing diameter compared to diameter "d" of main body portion 224E. The light then transmitted through the tip to receiving fiber optic 98'E passes through much less of the sample. This is desirable if the analyte to be detected is one of high density or has a higher extinguishing coefficient for the NIR and adjacent visible wavelengths in question. In the most extreme cases, fiber optics 98E and 98'E are moved down to the phantom position, 302, that reads through the narrowest part 304 of tip 48E.

[0067] Alternatively, passage of the NIR and adjacent visible radiation through the narrower part of the tip can be

achieved using previous embodiments, simply by raising the tip (and its probe) sufficiently within station 82, and then illuminating with the NIR radiation. Most preferably, the sequence of steps is as follows: the steps of lowering the tip into a light-tight enclosure comprising an NIR and adjacent visible radiation emitter as shown in any of Figs. 2A, 2B, 4A, and 4B until the tip is seated therein, scanning the tip and its contents with NIR and adjacent visible radiation emitted from the emitter, and if the contents have a density above a predetermined threshold value, thereafter raising the tip within the enclosure until the emitter is positioned to scan the narrower portion of the tip.

Claims

1. A method for improving throughput in a clinical analyser (12), the analyser (12) comprising a dispensing station (18) and at least one test station (82) for detecting a target substance in a patient sample, the dispensing station (18) comprising:

an aspirator probe (46);
a tip (48) mounted on the probe (46), for collecting a biological liquid from a primary collection container (19) and for dispensing at least a portion of the collected liquid onto or into a test element (E); and
means (71) for creating a partial pressure or partial vacuum within the probe (46) and the tip (48);

the method comprising the steps of:

a) aspirating a biological liquid into one of the tips (48) mounted on the probe (46);
b) while the liquid is within the tip (48) and the tip (48) is on the probe (46), receiving the tip (48) in a light-tight enclosure (82) connected to a spectrophotometer, detecting one or more target substances in the liquid by transmitting light of near infrared and adjacent visible radiation wavelengths through the tip (48) and spectrophotometrically analyzing the portion of the light transmitted through the tip (48), by correlating the transmitted light with the concentration of one or more target substances in the liquid;

the method being **characterised in that** it further comprises the steps of

c) dispensing a portion of the liquid from the tip (48) onto a test element (E); and
d) testing at the test station, the test element (E) plus liquid, for target substances other than the one or more target substances;

wherein the tip (48) comprises a wide portion and a narrower portion, and the step b) comprises the step of b') transmitting light through the narrower portion of the tip (48).

2. A method as defined in claim 1, wherein the liquid is selected from the group consisting of serum, plasma, whole blood, urine and cerebral spinal fluid.

3. A method as defined in claim 1 or 2, wherein step b) occurs after steps c) and d).

4. A method as defined in any one of claims 1 to 3, wherein the step b) comprises transmitting the light through the tip(48) in more than one pass.

5. A method as defined in any one of claims 1 to 4, wherein the step b') comprises moving the tip (48) within a light-tight enclosure, comprising an NIR and adjacent visible radiation emitter, so that the light transmitted by the emitter is directed through only the narrower portion.

6. A method as defined in claim 5, wherein the moving of the step b') comprises the steps of lowering the tip (48) into a light-tight enclosure comprising an NIR and adjacent visible radiation emitter until the tip is seated therein, scanning the tip (48) and its contents with NIR and adjacent visible radiation emitted from the emitter, and if the contents have a density above a predetermined threshold value, thereafter raising the tip (48) within the enclosure until the emitter is positioned to scan the narrower portion of the tip (48).

7. The method of claim 5 or claim 6, further including the step of preventing air pressurisation in the enclosed container when the tip (48) is moved or lowered into the light-tight enclosure, such as could disturb the liquid level within the tip (48).

8. The method of anyone of the preceding claims, wherein the target substance is selected from the group consisting of haemoglobin, lipids, bilirubin and biliverdin.

9. The method of claim 8, wherein the target substance is haemoglobin.

10. The method of any one of the preceding claims, wherein the tip is free of any identification labels.

11. A dispensing station (18) for use in a clinical analyser (12), comprising:

an aspirator probe (46);
a tip (48) mounted on the probe (46), for collecting a biological liquid from a primary collection container (19)
means (71) for creating a partial pressure or partial vacuum within the tip (48);
the station (18) further including a spectrophotometer (110) emitting near infrared and adjacent visible radiation and generating a signal responsive to portions of the radiation absorbed by any medium the radiation passes through;
a light-tight enclosure defining a cavity sized to receive the tip (48) while mounted on the probe (46);
passageways defining radiation paths to and from the enclosure from and to the spectrophotometer (110), the passageways being constructed to deliver and receive, respectively, the radiation for transmission through the tip (48) when the tip (48) is in place in the cavity, so that liquid in the tip (48) can be irradiated by the radiation to determine concentration of target substances therein;

characterised in that the tip is also for dispensing at least a portion of the collected liquid onto or into a test element (E) which is used for determining a target substance other than a target substance determined through the tip; and **in that** the enclosure includes walls and a vent in one of the walls effective to prevent a vacuum from occurring when the tip is removed from the enclosure.

12. A dispensing station as defined in claim 11, and further including a support for a test element (E) constructed to receive liquid dispensed from the tip (48), and means for moving the probe (46) and the tip (48) from the enclosure to the support for liquid dispensing after the radiation is transmitted through the tip (48).

13. A dispensing station as defined in claim 11 or 12, wherein the tip (48) is a disposable tip.

14. A dispensing station as defined in any one of claims 11 to 13, further including at least one pair of mirrors (230, 232; 270, 242; 250, 252) disposed within the cavity at a position to intercept radiation transmitted from one of the passageways through the tip (48) in single pass and to retransmit the radiation back through the tip (48) for the other of the passageways to receive it.

Patentansprüche

1. Verfahren, um den Durchsatz in einem klinischen Analysator (12) zu verbessern, wobei der Analysator (12) eine Verteilstation (18) und zumindest eine Teststation (82) zum Nachweis einer Zielsubstanz in einer Patientenprobe umfasst, wobei die Verteilstation (18):

- eine Saugsonde (46);
- eine auf die Sonde (46) montierte Spitze (48), um eine biologische Flüssigkeit aus einem ersten Sammelbehälter (19) aufzunehmen und um zumindest einen Teil der aufgenommenen Flüssigkeit auf oder in ein Testelement (E) zu verteilen; und
- Mittel (71), um einen teilweisen Druck oder ein teilweises Vakuum innerhalb der Sonde (46) und der Spitze (48) zu erzeugen;

umfasst;
wobei das Verfahren die Schritte:

a) Ansaugen einer biologischen Flüssigkeit in eine von den auf der Sonde (46) montierten Spitzen (48);
b) Aufnehmen der Spitze (48) in eine mit einem Spektrometer verbundene lichtdichte Umhüllung (82), während die Flüssigkeit innerhalb der Spitze (48), und die Spitze (48) auf der Sonde (46) ist,

Nachweis von einer oder mehreren Zielsubstanzen in der Flüssigkeit durch Durchleiten von Licht des nahen Infrarot und zu sichtbarem Licht benachbarten Strahlungswellenlängen durch die Spitze (48) und spektrophotometrisches Analysieren des Bereichs des Lichts, das durch die Spitze (48) transmittiert wird, durch Korrelation des transmittierten Lichts mit der Konzentration einer oder mehrerer Zielsubstanzen in der Flüssigkeit; umfasst;

wobei das Verfahren **dadurch gekennzeichnet ist, dass** es ferner die Schritte umfasst:

c) Verteilen eines Teils der Flüssigkeit von der Spitze (48) auf ein Testelement (E); und
d) Testen des Testelements (E) plus Flüssigkeit an der Teststation auf andere Zielsubstanzen als die eine oder mehreren Zielsubstanzen;

wobei die Spitze (48) einen breiten Abschnitt und einen schmaleren Abschnitt umfasst, und der Schritt b) den Schritt b'), Transmittieren von Licht durch den schmaleren Abschnitt der Spitze (48), umfasst.

2. Verfahren nach Anspruch 1, wobei
die Flüssigkeit aus der Gruppe, bestehend aus Serum, Plasma, Vollblut, Urin und zerebraler Spinalflüssigkeit, ausgewählt wird.

3. Verfahren nach Anspruch 1 oder 2, wobei
Schritt b) nach den Schritten c) und d) eintritt.

4. Verfahren nach einem der Ansprüche 1 bis 3, wobei
der Schritt b) das Transmittieren von Licht durch die Spitze (48) in mehr als einem Durchgang umfasst.

5. Verfahren nach einem der Ansprüche 1 bis 4, wobei
der Schritt b') das Bewegen der Spitze (48) innerhalb einer lichtdichten Umhüllung umfasst, umfassend einen Sender für NIR und für zu sichtbarer Strahlung benachbarte Strahlung, so dass das Licht, das von dem Sender transmittiert wird, nur durch den schmaleren Abschnitt gelenkt wird.

6. Verfahren nach Anspruch 5, wobei
das Bewegen des Schritts b') die Schritte des Absenkens der Spitze (48) in eine lichtdichte Umhüllung, umfassend einen Sender für NIR und für zu sichtbarer Strahlung benachbarte Strahlung, bis die Spitze darin abgesetzt ist, des Scannens der Spitze (48) und ihres Inhalts mit von dem Sender abgestrahlter NIR-Strahlung und mit zu sichtbarer Strahlung benachbarter Strahlung, und, falls der Inhalt eine Dichte über einem vorab bestimmten Grenzwert aufweist, des anschließenden Hebens der Spitze (48) innerhalb der Umhüllung, bis der Sender positioniert ist, um den schmaleren Abschnitt der Spitze (48) zu scannen, umfasst.

7. Verfahren nach Anspruch 5 oder 6, ferner enthaltend
den Schritt des Verhinderns der Druckbeaufschlagung in dem abgeschlossenen Behälter, die das Flüssigkeitsniveau innerhalb der Spitze (48) stören könnte, wenn die Spitze (48) in die lichtdichte Umhüllung bewegt oder gesenkt wird.

8. Verfahren nach einem der vorangehenden Ansprüche, wobei
die Zielsubstanz aus der Gruppe, bestehend aus Hämoglobin, Lipiden, Bilirubin und Biliverdin, ausgewählt wird.

9. Verfahren nach Anspruch 8, wobei
die Zielsubstanz Hämoglobin ist.

10. Verfahren nach einem der vorangehenden Ansprüche, wobei
die Spitze frei von irgendwelchen Identifizierungszeichen ist.

11. Verteilstation (18) zur Benutzung in einem klinischen Analysator (12), umfassend:

- eine Saugsonde (46);
- eine auf die Sonde (46) montierte Spitze (48), um eine biologische Flüssigkeit aus einem ersten Sammelbehälter (19) aufzunehmen;
- Mittel (71), um einen teilweisen Druck oder ein teilweises Vakuum innerhalb der Spitze (48) zu erzeugen;

wobei die Station (18) ferner enthält

- ein Spektrophotometer (110), das nahes Infrarot und zu sichtbarer Strahlung benachbarte Strahlung aussendet und das ein Signal erzeugt, das anspricht auf Bereiche der durch irgendein Medium absorbierten Strahlung, durch das die Strahlung hindurchtritt;
- eine lichtdichte Umhüllung, die einen Hohlraum definiert, bemessen, um die Spitze (48), während sie auf der Sonde (46) montiert ist, aufzunehmen;
- Durchgangswege, die Strahlungswege zu und von der Umhüllung und von und zu dem Spektrophotometer (110) definieren, wobei die Durchgangswege konstruiert sind, um die Strahlung für die Transmission durch die Spitze (48) zu liefern bzw. zu empfangen, wenn die Spitze (48) in dem Hohlraum plaziert ist, so dass Flüssigkeit in der Spitze (48) durch die Strahlung bestrahlt werden kann, um Konzentrationen von Zielsubstanzen darin zu bestimmen; **dadurch gekennzeichnet, dass**
- die Spitze auch zum Verteilen von zumindest einem Teil der aufgenommenen Flüssigkeit auf oder in ein Testelement (E), das benutzt wird, um eine andere Zielsubstanz als eine Zielsubstanz, die über die Spitze bestimmt wird, zu bestimmen; und
- dass die Umhüllung Wände und eine Entlüftung in einer von den Wänden enthält, die bewirkt, dass ein Auftreten eines Vakuums verhindert wird, wenn die Spitze von der Umhüllung entfernt wird.

12. Verteilstation nach Anspruch 11, ferner enthaltend einen Träger für ein Testelement (E), konstruiert, um Flüssigkeit aufzunehmen, die von der Spitze (48) verteilt wird, und Mittel, um die Sonde (46) und die Spitze (48) von der Umhüllung zu dem Träger zu bewegen, um die Flüssigkeit zu verteilen, nachdem die Strahlung durch die Spitze (48) transmittiert wurde.

13. Verteilstation nach Anspruch 11 oder 12, wobei die Spitze (48) eine wegwerfbare Spitze ist.

14. Verteilstation nach einem der Ansprüche 11 bis 13, ferner enthaltend zumindest ein Paar von Spiegeln (230, 232; 270, 242; 250, 252), die innerhalb des Hohlraums an einer Position aufgestellt sind, um die Strahlung, die von einem der Durchgangswege transmittiert wird durch die Spitze (48) in einem einmaligen Durchtritt zu unterbrechen und um die Strahlung zurück durch die Spitze (48) für die anderen der Durchgangswege wieder auszusenden, damit diese sie aufnehmen.

Revendications

1. Procédé pour améliorer le débit dans un analyseur clinique (12), l'analyseur (12) comprenant un poste de distribution (18) et au moins un poste d'analyse (82) pour détecter une substance cible dans l'échantillon d'un patient, le poste de distribution (18) comprenant :

une sonde d'aspiration (46) ;
un embout (48) monté sur la sonde (46), pour recueillir un liquide biologique à partir d'un récipient de collecte principal (19) et pour distribuer au moins une partie du liquide recueilli sur ou dans un élément test (E) ; et
des moyens (71) pour créer une pression partielle ou un vide partiel à l'intérieur de la sonde (46) et de l'embout (48) ;

le procédé comprenant les étapes consistant à :

a) aspirer un liquide biologique dans l'un des embouts (48) montés sur la sonde (46) ;
b) lorsque le liquide est à l'intérieur de l'embout (48) et que l'embout (48) est sur la sonde (46), recevant l'embout (48) dans un boîtier opaque (82) relié à un spectrophotomètre, détecter une ou plusieurs substances cibles dans le liquide en émettant de la lumière de longueurs d'onde du rayonnement proche infrarouge et visible adjacent à travers l'embout (48) et analyser par spectrophotomètre la partie de la lumière émise à travers l'embout (48), en mettant en corrélation la lumière émise avec la concentration d'une ou de plusieurs substances cibles dans le liquide ;

le procédé étant **caractérisé en ce qu'**il comprend en outre les étapes consistant à :

c) distribuer une partie du liquide à partir de l'embout (48) sur un élément test (E) ; et

d) analyser au niveau du poste d'analyse, l'élément test (E) plus le liquide, pour trouver les substances cibles autres que la ou les substances cibles ;

dans lequel l'embout (48) comprend une partie large et une partie plus étroite, et l'étape b) comprend l'étape b') consistant à émettre de la lumière à travers la partie plus étroite de l'embout (48).

2. Procédé selon la revendication 1, dans lequel le liquide est choisi dans le groupe comprenant du sérum sanguin, du plasma sanguin, du sang total, de l'urine et du liquide céphalorachidien.

3. Procédé selon la revendication 1 ou la revendication 2, dans lequel l'étape b) est réalisée après les étapes c) et d).

4. Procédé selon l'une quelconque des revendications 1 à 3, dans lequel l'étape b) comprend l'émission de la lumière à travers l'embout (48) sur plus d'un passage.

5. Procédé selon l'une quelconque des revendications 1 à 4, dans lequel l'étape b') comprend le déplacement de l'embout (48) à l'intérieur d'un boîtier opaque, comprenant un émetteur de rayonnement proche infrarouge et adjacent au visible, de sorte que la lumière émise par l'émetteur soit dirigée uniquement à travers la partie plus étroite.

6. Procédé selon la revendication 5, dans lequel le déplacement de l'étape b') comprend les étapes consistant à abaisser l'embout (48) dans un boîtier opaque comprenant un émetteur de rayonnement proche infrarouge et adjacent au visible jusqu'à ce que l'embout soit posé à l'intérieur de celui-ci, balayer l'embout (48) et son contenu au moyen du rayonnement proche infrarouge et adjacent au visible émis de l'émetteur, et si le contenu a une densité au-dessus d'une valeur seuil prédéterminée, remonter par la suite l'embout (48) à l'intérieur du boîtier jusqu'à ce que l'émetteur soit positionné de manière à balayer la partie plus étroite de l'embout (48).

7. Procédé selon la revendication 5 ou la revendication 6, comprenant en outre l'étape consistant à empêcher une pressurisation de l'air dans le boîtier fermé lorsque l'embout (48) est déplacé ou abaissé à l'intérieur du boîtier opaque, qui pourrait perturber le niveau du liquide à l'intérieur de l'embout (48).

8. Procédé selon l'une quelconque des revendications précédentes, dans lequel la substance cible est choisie dans le groupe comprenant l'hémoglobine, les lipides, la bilirubine et la biliverdine.

9. Procédé selon la revendication 8, dans lequel la substance cible est l'hémoglobine.

10. Procédé selon l'une quelconque des revendications précédentes, dans lequel l'embout ne présente aucune étiquette d'identification.

11. Poste de distribution (18) pour une utilisation dans un analyseur clinique (12), comprenant :

une sonde d'aspiration (46) ;
un embout (48) monté sur la sonde (46), pour recueillir un liquide biologique à partir d'un récipient de collecte principal (19) ;
des moyens (71) pour créer une pression partielle ou un vide partiel à l'intérieur de l'embout (48) ;
le poste (18) comprenant en outre un spectrophotomètre (110) émettant un rayonnement proche infrarouge et adjacent au visible et produisant un signal sensible aux parties du rayonnement absorbées par tout milieu à travers lequel passe le rayonnement ;
un boîtier opaque définissant une cavité dimensionnée pour recevoir l'embout (48) lorsqu'il est monté sur la sonde (46) ;
des passages définissant des trajectoires de rayonnement vers et à partir du boîtier à partir de et vers le spectrophotomètre (110), les passages étant élaborés pour émettre et recevoir, respectivement, le rayonnement pour une émission à travers l'embout (48) lorsque l'embout (48) est en place dans la cavité, de manière à ce que le liquide dans l'embout (48) puisse être irradié par le rayonnement pour déterminer la concentration des substances cibles à l'intérieur de celui-ci ;

caractérisé en ce que l'embout permet également de distribuer au moins une partie du liquide recueilli sur ou dans un élément test (E) qui est utilisé pour déterminer une substance cible autre qu'une substance cible déterminée à travers l'embout ; et

en c que le boîtier comprend des parois et un conduit sur l'une des parois apte à empêcher qu'un vide ne

se produise lorsque l'embout est retiré du boîtier.

12. Poste de distribution selon la revendication 11, comprenant en outre un support pour un élément test (E) élaboré pour recevoir du liquide distribué à partir de l'embout (48), et des moyens pour déplacer la sonde (46) et l'embout (48) à partir du boîtier vers le support pour une distribution du liquide après que le rayonnement ait été transmis à travers l'embout (48).

13. Poste de distribution selon la revendication 11 ou la revendication 12, dans lequel l'embout (48) est un embout jetable.

14. Poste de distribution selon l'une quelconque des revendications 11 à 13, comprenant en outre au moins une paire de miroirs (230, 232 ; 270, 242 ; 250, 252) disposée à l'intérieur de la cavité à un emplacement pour intercepter le rayonnement transmis à partir de l'un des passages à travers l'embout (48) en un seul passage et pour retransmettre en retour le rayonnement à travers l'embout (48) pour que les autres passages puissent le recevoir.

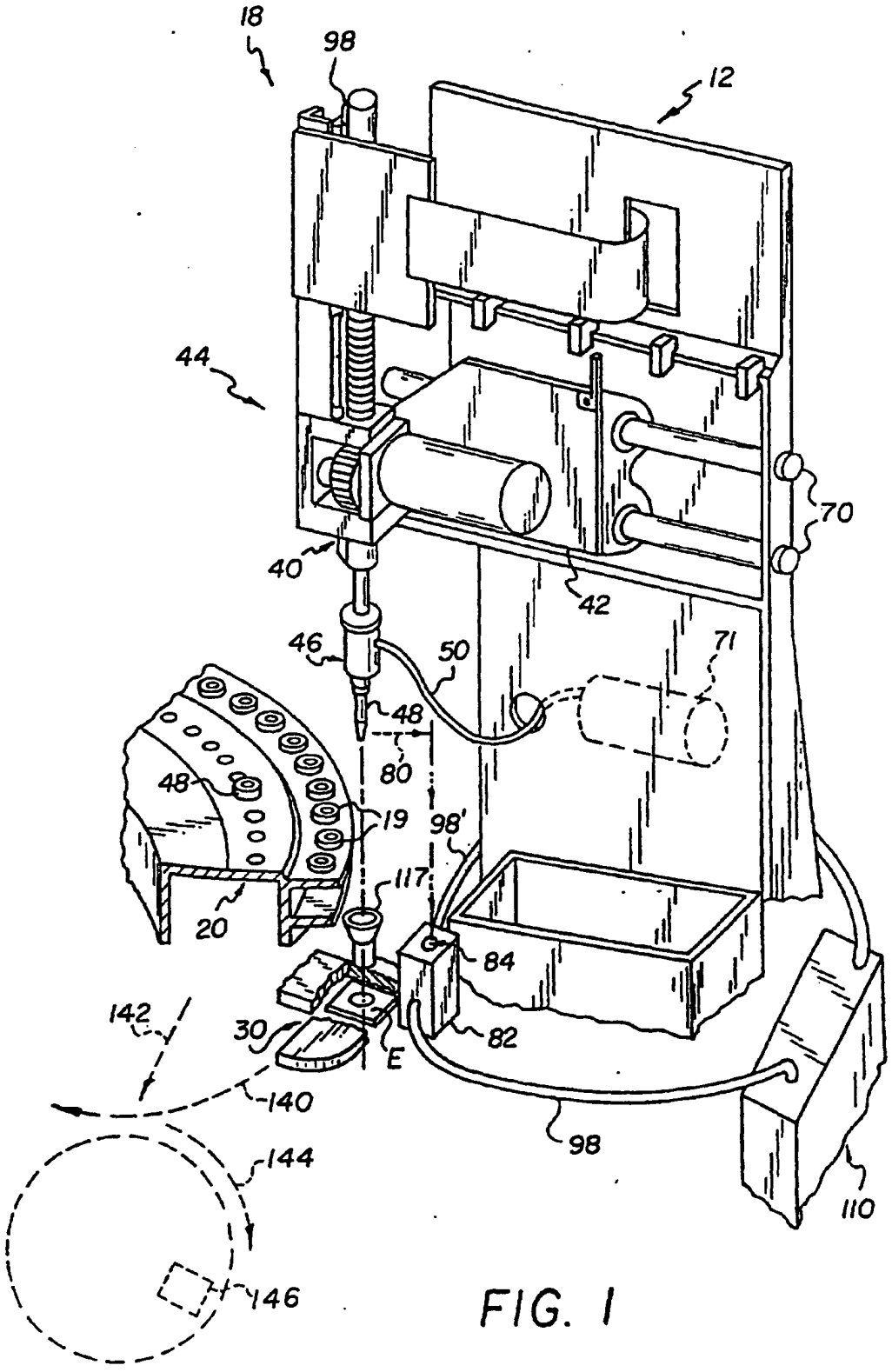
18
98
12
44
70
40
42
46
50
71
48
80
48
19
98'
117
20
84
142
30
E
82
140
144
98
110
146

FIG. 1

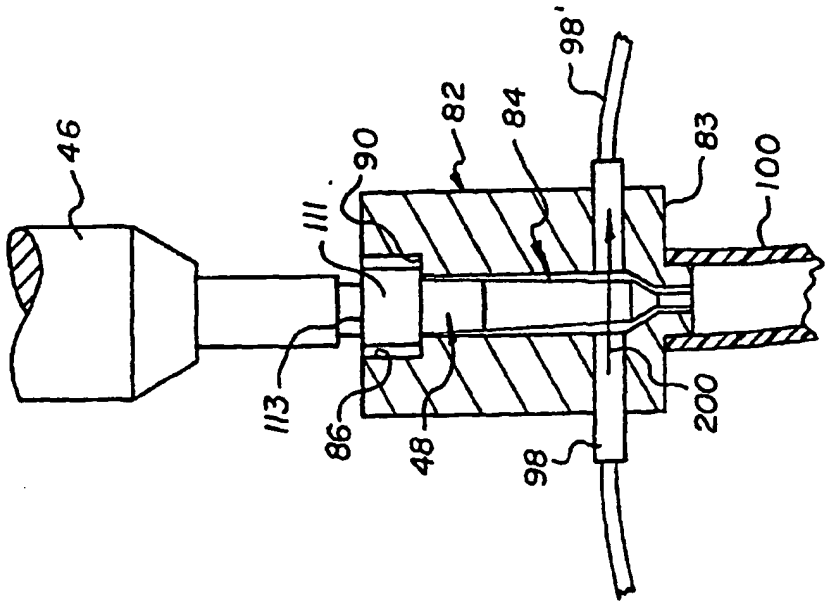
46
90
111
82
84
98'
83
100
113
86
48
98
200

FIG. 2B

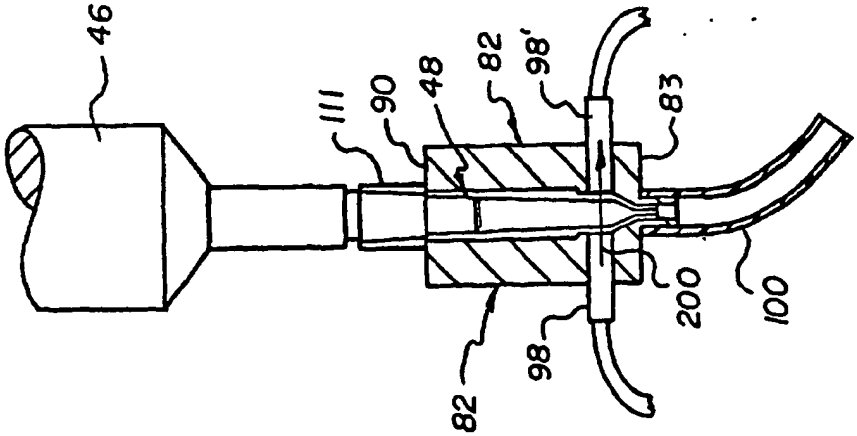
46
111
90
48
82
98'
83
200
100
98
82

FIG. 2A

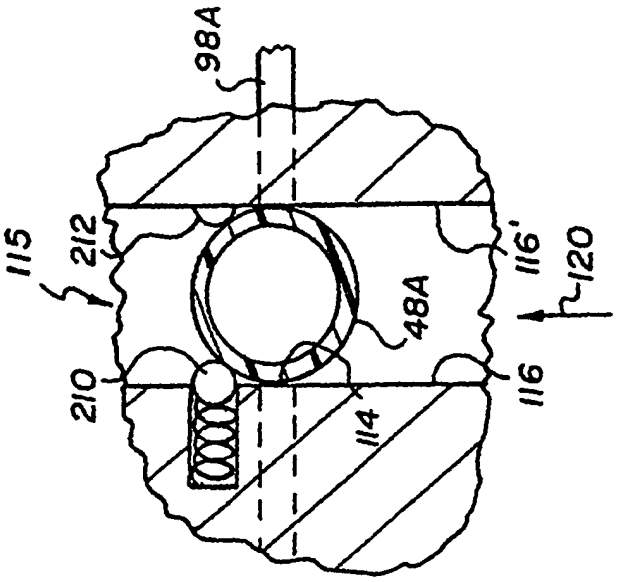

FIG. 5

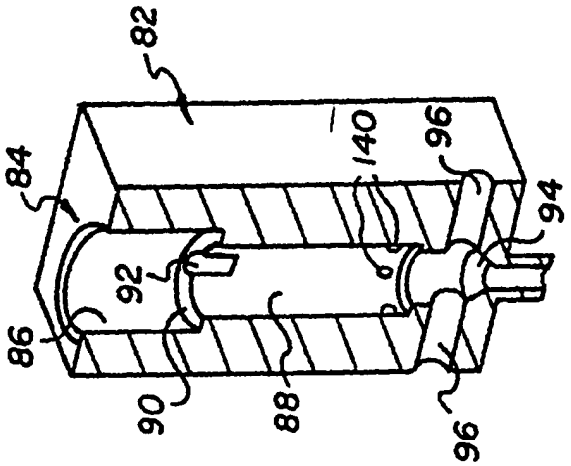

FIG. 3

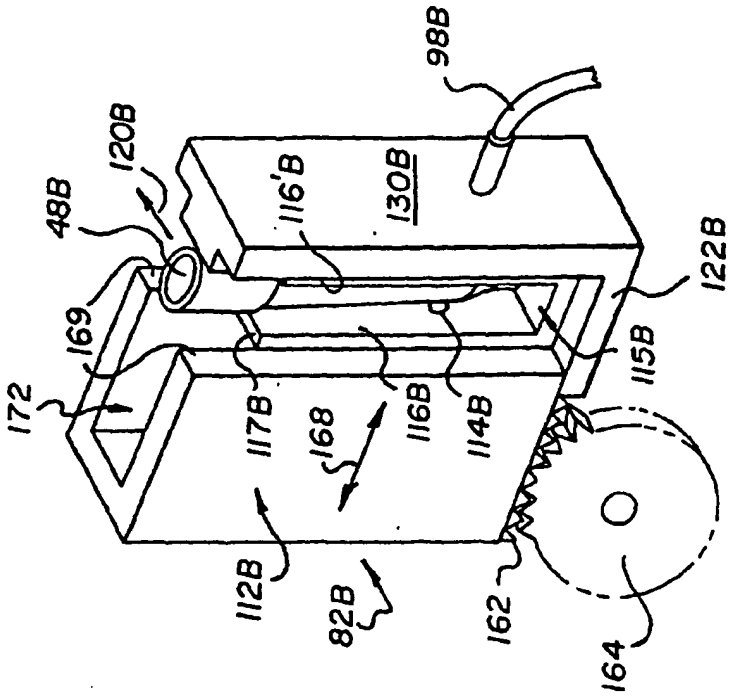
98B
120B
48B
116'B
130B
122B
169
115B
172
117B
168
116B
114B
112B
82B
162
164

FIG. 4B

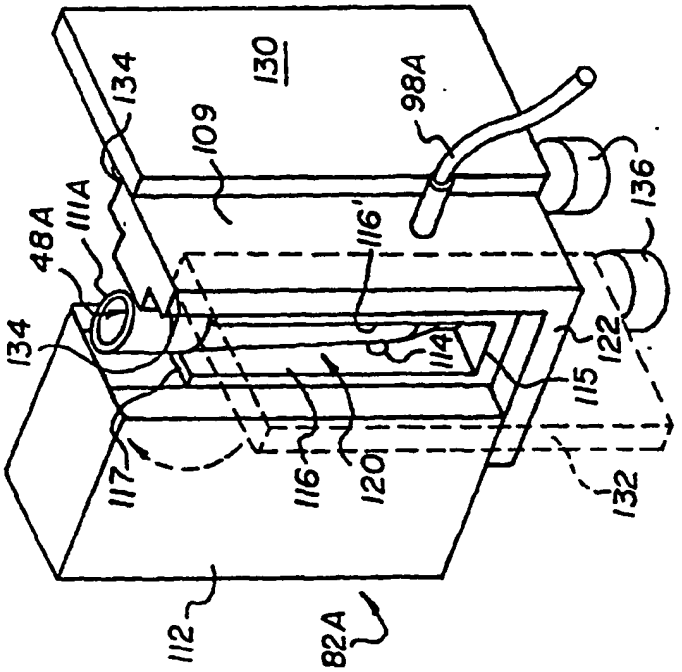
130
134
98A
109
136
48A
111A
116'
134
114
122
115
117
116
120
132
112
82A

FIG. 4A

HEMOBLOBIN REPREDICTION OF CALIBRATION FLUIDS

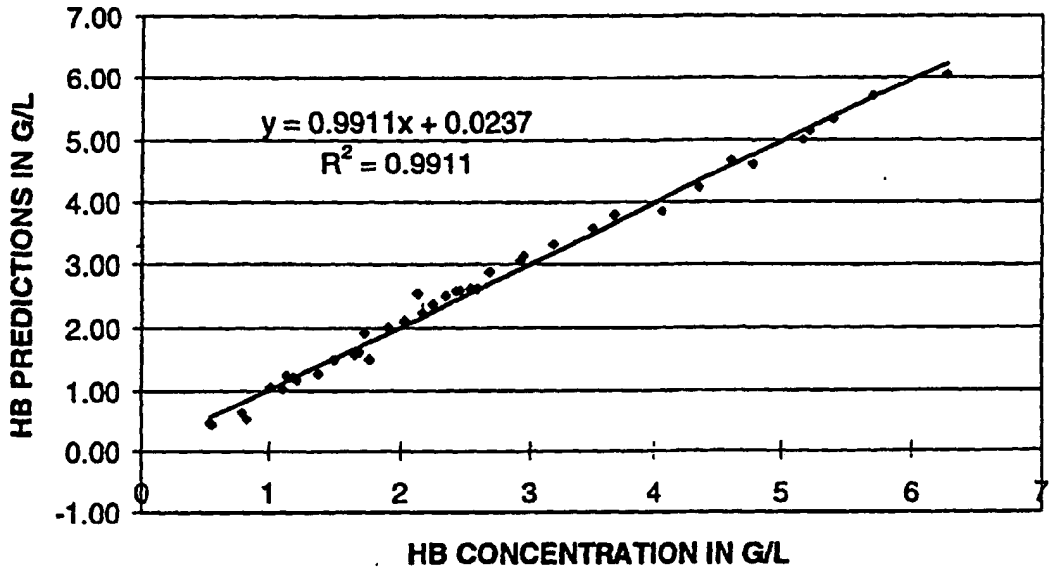

FIG. 6

HEMOBLOBIN REPREDICTION OF UNKNOWN FLUIDS

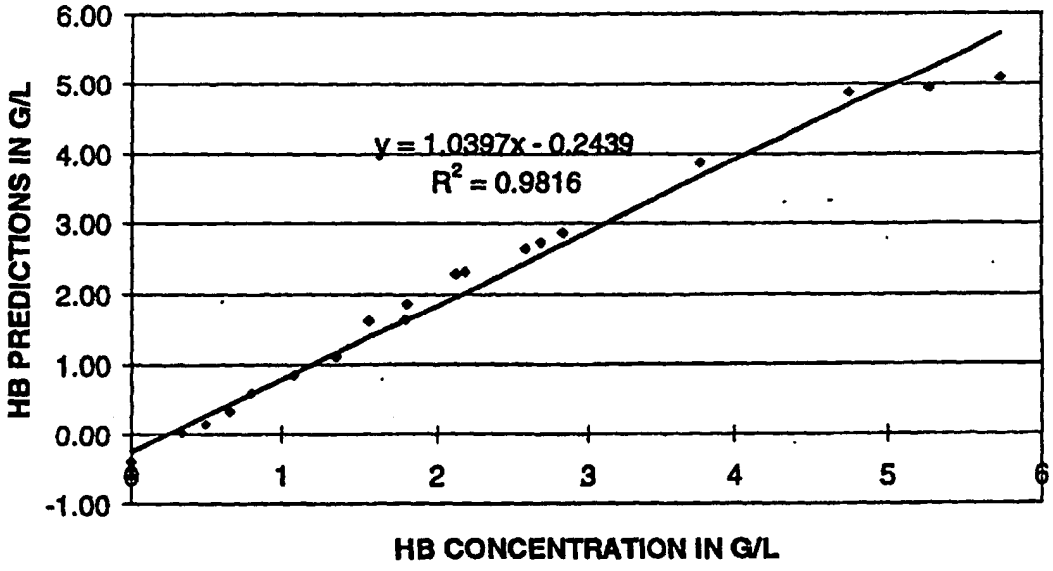

FIG. 7

INTRALIPID REPREDICTION OF CALIBRATION FLUIDS

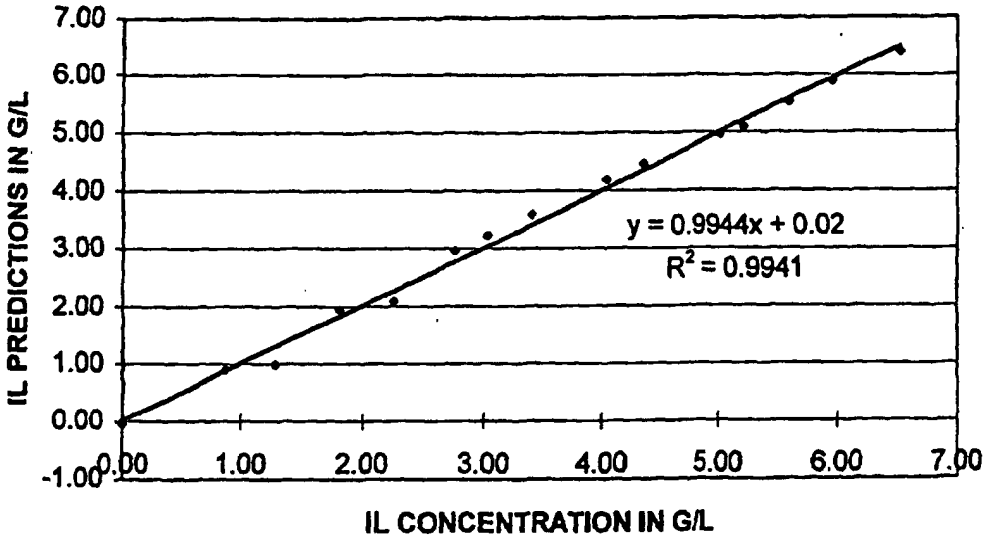

FIG. 8

INTRALIPID REPREDICTION OF UNKNOWNS FLUIDS

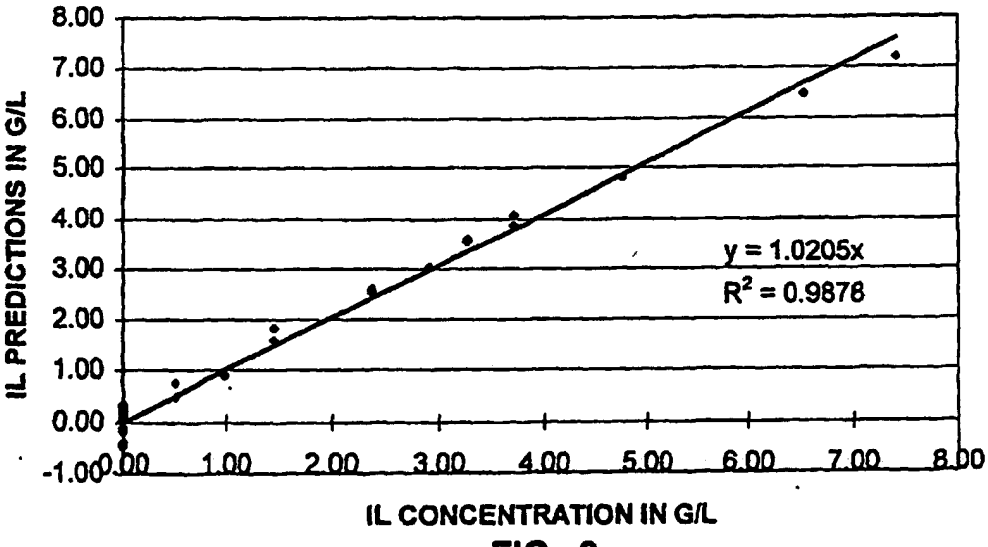

FIG. 9

BILIVERDIN REPREDICTION OF CALIBRATION FLUIDS

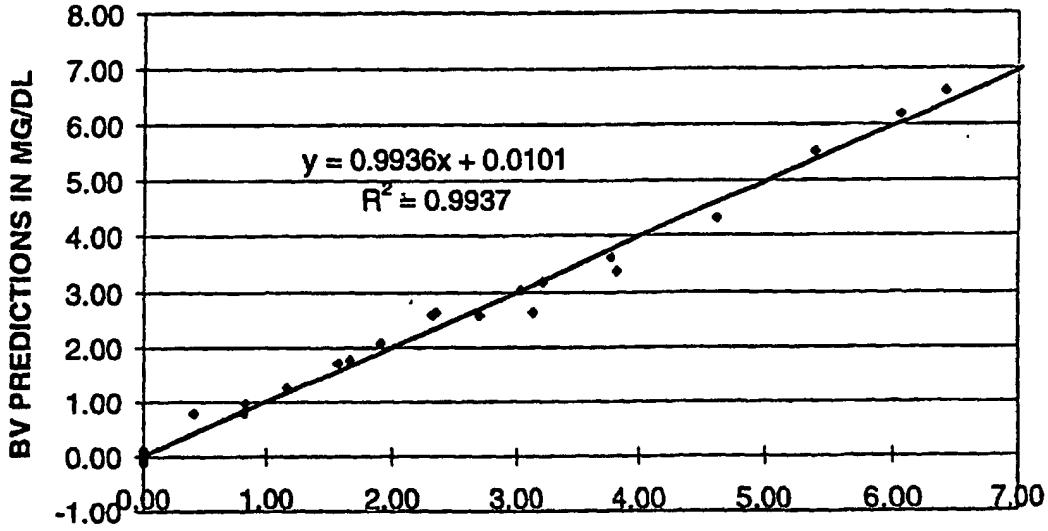

FIG. 10

BILIVERDIN REPREDICTION OF UNKNOWN FLUIDS

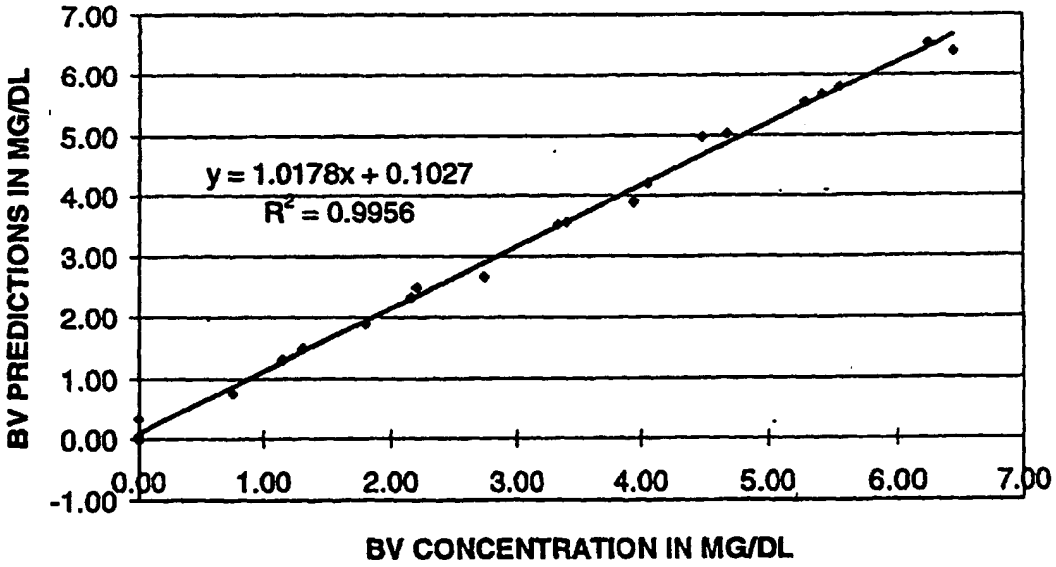

FIG. 11

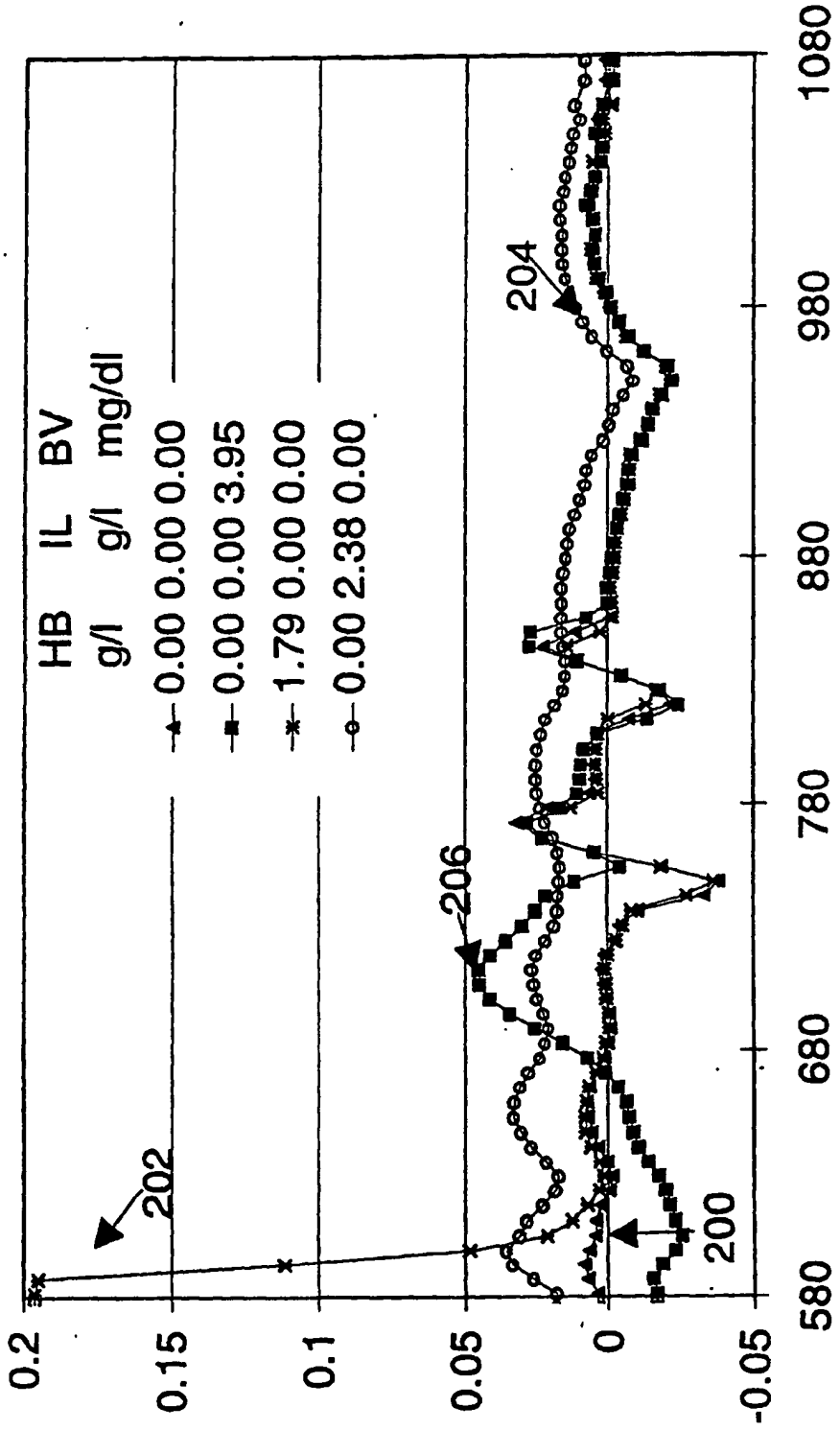
HB IL BV
g/l g/l mg/dl
0.00 0.00 0.00
0.00 0.00 3.95
1.79 0.00 0.00
0.00 2.38 0.00
202
204
206
200
0.2
0.15
0.1
0.05
0
-0.05
580
680
780
880
980
1080
wavelength (nm)
First derivative of absorbance

Fig. 12

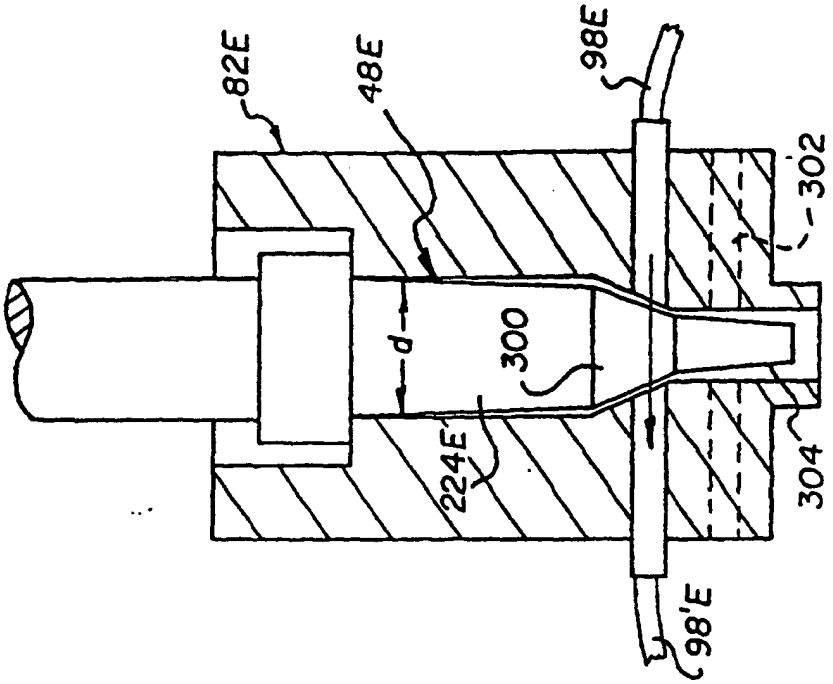
82E
48E
98E
302
d
300
224E
304
98'E

FIG. 14

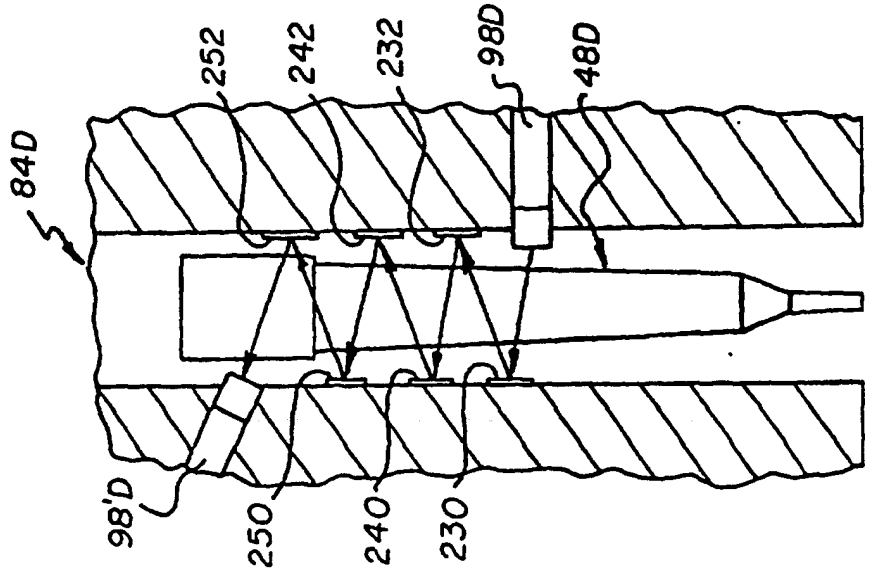
84D
252
242
232
98D
48D
98'D
250
240
230

FIG. 13

BILIRUBIN REPREDICTION OF CALIBRATOR FLUIDS

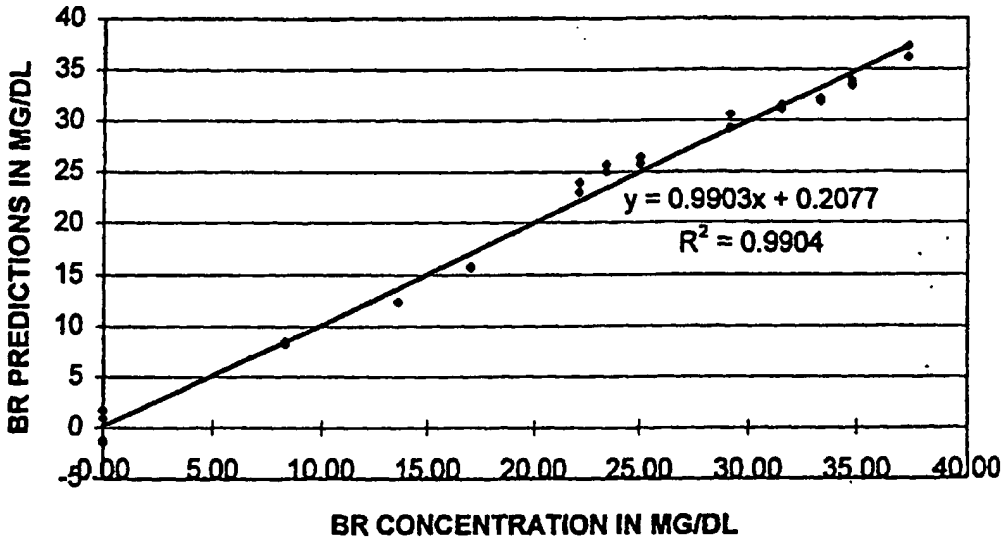

FIG. 15

BILIRUBIN REPREDICTION OF UNKNOWN FLUIDS

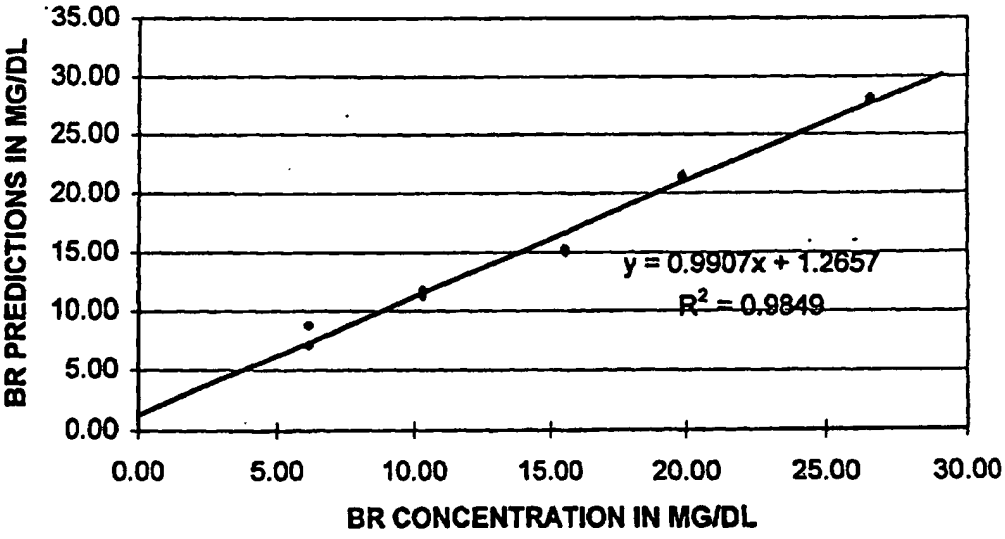

FIG. 16